

Patterns of Presentation and Management of Differentiated Thyroid Cancer at the National Cancer Institute - Central Sudan

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Abstract: **Background:** Thyroid cancer is the second most common cause of mortality amongst endocrine malignancies, after ovarian cancer. Thyroid tumors that are differentiated account for around 95% of all thyroid malignancies. Thyroid cancer now outnumbers all other cancers in terms of occurrence. **Objective:** The study aimed to investigate the pattern of presentation and management of differentiated thyroid cancer at the National Cancer Institute in Wad Medani, Gezira State–Sudan. **Methods:** This is a retrospective descriptive hospital-based research that included all patients with differentiated thyroid carcinoma who presented to the National Cancer Institute Wad Medani between September 2016 and September 2020. The information is gathered using a standard structured data collection sheet and evaluated with SPSS for scientific class packaging for the social meaning of statistical packaging for social sciences version 24, USA. **Results:** Females 56 (76%) out of 74 patients with differentiated thyroid carcinoma at the National Cancer Institute Wad Medani had a male-to-female ratio of 1:3.2, and 18 of them (24.3%) were in the 41-50 year age category. Sixty-nine (93.2%) of patients exhibited anterior neck swelling, whereas 15 (20.3%) reported shortness of breath. Sixty-six (89.2%) of patients had euthyroid status, and forty-nine (66.2%) had multinodular findings on ultrasonography, while the lateral compartment of lymph nodes was implicated in 8 (10.8 %) patients, the lateral and central compartments were engaged in 6 (8.1 %) patients, and the rest of the patients had no affected lymph nodes, 60 (81.1 %) had cold nodules on radioisotope scan, and 63 (85.1%) had cold nodules. Long-term goiter, which was reported in 20 of the research subjects, was the most prevalent risk factor (27 %). Papillary carcinoma is the most common histological form, accounting for 38.4% of all cases. Were 41(55%) with TNM stage-I. The scalp is the first site of metastases 6 (8.1%) in eighteen (24.3%) cases. The 38.4% of the patients had a total thyroidectomy, which was proceeded by radioactive iodine therapy in 47.4% of the cases. **Conclusion:** Early thyroid cancer identification is critical for effective management of differentiated thyroid carcinoma.

Keywords: Thyroid cancer; National Cancer Institute; Wad Medani; Sudan.

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INTRODUCTION

The most common endocrine cancer among women is thyroid cancer. Thyroid cancer comes in a variety of types, ranging from well-differentiated to undifferentiated. Thyroid carcinomas generated from follicular epithelial cells, such as papillary, follicular, and Hurthle cell carcinomas, are categorized as well

differentiated thyroid tumors and account for the vast majority of thyroid cancers [1].

Thyroid cancer accounts for 1–5% of all cancers globally. Every year, more cases of thyroid cancer are identified, thanks to better diagnostic methods such as high-resolution ultrasonography. The majority of thyroid cancers are well-differentiated

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thyroid tumors. Thyroid carcinoma that has been differentiated has a 10-year survival rate of between 85 and 95 %. Patients with distant metastases have a 50% chance of survival [2].

Thyroid cancer impacts around 37,000 people in the United States annually, placing tenth among solid organ cancers in terms of incidence. Thyroid cancer has increased 2.4-fold from 1973 to 2002, despite the fact that the yearly rate of cancer incidence is decreasing. The cause of inflation is uncertain, but the tendency is continuing. Thyroid cancer has a substantial female prevalence (2.7:1). The majority of thyroid tumors are categorized as papillary (88%) or follicular (9%); these two histological categories are combined to form differentiated thyroid tumors. Because they have comparable clinical treatment, they will be explored jointly [3].

The most common symptom of differentiated thyroid cancer is an increase in the size of the thyroid gland or other neck enlargement; however, in a small percentage of instances, patients appear with unusual symptoms, and an examination reveals thyroid cancer with distant metastases. As uncommon as the cases is the literature on this issue [2].

Despite the fact that differentiated thyroid tumors has a better prognosis than other tumors, optimal results can only be attained by integrated multimodal therapy. Surgery is the cornerstone of initial care for all of these procedures. Thyroidectomy with central neck (level VI) lymph node dissection is recommended for the majority of patients. Thyroidectomy alone, on the other hand, may be suitable for individuals with smaller tumors (T1 or T2) and no worrisome lymphadenopathy. In instances of cervical lymph node metastases and locoregional recurrence, surgery is also considered. Radioactive iodine is the most common adjuvant treatment, and it should be explored in patients with a high risk of locoregional recurrence or metastatic malignancy. In individuals with a high risk of recurrence, inhibition of endogenous thyroid-stimulating hormone is also advocated. Patients with extensive extrathyroidal expansion or residual cancer that is not responsive to surgery should consider external-beam radiotherapy. Finally, molecular treatments, particularly those that target critical tyrosine kinases and/or restrict angiogenesis, are developing therapeutic options that might replace traditional chemotherapy's low effectiveness [4].

PATIENTS AND METHODS

Study design, Study area, and duration

This hospital-based study is a one-year prospective and three-year retrospective descriptive study. The study was performed at the National Cancer Institute (NCI) in Wad Medani, Sudan's Gazira State. In 1994, the National Cancer Institute was founded as

Sudan's second nuclear medicine and molecular biology institution. The institution added an oncology department in 1999. The catchment area included states in the country's centre and eastern regions. All patients with surgical malignancies are evaluated and treated in a combination clinic held twice weekly by a surgeon, oncologist, radiologist, and pathologist. NCI offers a wide range of anti-cancer treatments, including radiation, chemotherapy, and hormone therapy. The research was conducted out between September 2016 and September 2020.

Study population and sample size

All patients with differentiated thyroid cancer (DTC) who visited the National Cancer Institute Wad Medani throughout the research period were included. All participants who had been diagnosed with DTC were included in the study.

Exclusion and inclusion criteria

Patients with other types of thyroid cancer, those with insufficient data, and those who declined to participate were all excluded from the study, while all patients with DTC were included.

DATA COLLECTION TOOLS AND METHODS

The lead investigator gathered data by interviewing patients and evaluating their medical records. Structured questionnaires were used to collect data on demographics, clinical presentations, examinations, investigations, tissue diagnosis, metastasis, and management patterns, as well as consequences.

Study variables

Socio-demographic characteristics of participants: age, gender, residence - Presenting features. Risk factors - Examinations - Investigations - Tissue diagnosis (pattern) - DTC stages - Tumor size - Lymph nodes status - Metastasis - Types of management - Complications.

DATA ANALYSIS

Data retrieved from National Cancer Institute (NCI) was transferred to Excel spread sheet (Microsoft Corp). The data was subsequently cleaned, recoded and analyzed using IBM SPSS Statistical package version 24.0 (Armonk, New York, USA). Study variables were expressed as numbers. Pearson Chi-square (χ^2) test was used to evaluate the relationship between categorical variants. A p - value <0.05 was considered statistically significant.

ETHICAL CONSIDERATION

Sudan's medical specialized board granted ethical approval (SMSB). The hospital authority was awarded approval acceptance. Patients gave their written and verbal permission. To safeguard the patient's identify, data is anonymized by utilizing identity numbers instead of names, and it is maintained

securely and in a separate file. There is no mention of any particular participant in the study reports. Only the study staff was aware of the subjects' identities.

RESULTS

A total of 74 patients with differentiated thyroid carcinoma were recruited in our study, the plurality of them were in the age category 41-50 years, with 56 (76%) being females and 18 (24%) being males. The most of the patients 48% were from central Sudan (64.9%) (Table 1).

Anterior neck swelling was the predominant presentation in 69 (93.2%); with shortness of breath was report in 15 (20.3%); while sudden size increasing reported in 9 (12.2%) in more than 10% of the patients. Long standing goiter (n=20; 27%), previous surgery (n=4; 5.4%) and family history of thyroid cancer (n=4; 5.4%) were the main encountered risk factors, while the remaining 46(62.2%) patients did not have any risk factors (table 2).

Majority of the patients were euthyroid in 66 (89.2%). In ultrasonography, there were 49 (66.2%) multinodular findings. Cold radioisotopes were found in 63 (85.1%) of the patients. 38 patients (51.4%) had papillary carcinoma, 33 (44.6%) had follicular carcinoma, and 3 (4.1%) had Hurthles carcinoma, according to histological diagnosis (table3).

The most prevalent stage of the patients was stage I, which accounted for 41 of them (55 %). The majority of the patients (33 %, or 44.6 %) had tumors of 1-2 cm in size. Ultrasound revealed lymph node involvement in 8(10.8%) patients, lateral compartment involvement in 6(8.1%) patients, and lateral and central compartment involvement in 6(8.1%) patients, and the rest of the patients 60(81.1%) had no affected lymph nodes. Metastasis was identified in 18 (24.3%) of the patients, including 12 (16.2%) in the bone, 4 (5.4%) in the lung, and 2 (2.4%) in the lymph nodes (table 4).

In terms of treatment, the majority of patients (38.4%) received complete thyroidectomy, 16 (21.6%) underwent completion following lobectomy, 14 (18.9%) received near complete thyroidectomy, and 2 (2.7%) got debulking, while 4(5.4%) patients did not underwent any surgery. There were no intraoperative difficulties, however six patients suffered postoperative

issues, including persistent vocal cord palsy in three (4.1%), transitory vocal cord palsy in two (2.7%), and surgical site infection in one (1.4%) patient. Radioactive iodine was utilized as an adjuvant therapy in 47 patients (63.4%), radiation in 6 patients (8.1%), chemotherapy in one patient (1.4%), and combination treatment in 13 patients (17.6 %). While the remaining 7 (9.5%) received only high-dose thyroxin as adjuvant treatment (table 5).

.When comparing the relationship between metastases and histological type, follicular metastases were the most common, with bone metastases being the most common site, while papillary metastases were second, with bone metastases being the most common site, and both of these relationships were statistically significant (P. value 0.010) (table 3).

In regard to postoperative complication permanent vocal cord palsy occurred in three of total patients, each one of them underwent different types of operation (total thyroidectomy, near total thyroidectomy and in completion surgery), while transient vocal cord paralysis occurred only in 2 patients underwent total thyroidectomy and surgical site infection occurred in one patient who also underwent total thyroidectomy, this relation showed that total thyroidectomy has been associated with most of complications that founded in this study though this finding statistically is insignificant (P value 0.986) (table 5).

In relation of the age group to histological type we founded that papillary and follicular were most common in age group (51-60), this relations were statistically is insignificant (P value 0.500)(table 1).

Female patients had an equal distribution of papillary and follicular histological types as compared to gender distribution (27 each) (P value 0. 535) and statistically was insignificant (table 6).

Long-term goiter was the most well-established risk factor, which was linked to papillary (10), follicular (8), and hurthle (2) histological types of DTC, but the majority of patients had no risk factor, despite the statistical insignificance of this relationship(P value 0.078) it is appear to have clinical significance (table 6).

Table-1: Age, residency and age in relation to histological type

Variable	Parameter	Tissue type			Frequency	Percent %	P value
		Papillary	Follicular	Hurthles			
Age group (Years)	10-20	2	0	0	2	2.7	0.500
	21-30	4	3	0	7	9.5	
	31-40	5	4	0	9	12.2	
	41-50	13	4	1	18	24.4	
	51-60	6	9	1	16	21.6	
	61-70	5	8	1	14	18.9	
	>70	3	5	0	8	10.8	
Residence	Central				48	64.9	
	East				19	25.2	
	North				4	5.4	
	South				3	4.1	

Table-2: Clinical feature, risk factor, and examination of study participants

Variable	Parameter	Frequency	Percent %
Clinical feature	Anterior neck swelling	69	93.2
	Breathing difficulty	15	20.3
	Sudden increase in size	7	9.5
	Hoarseness of voice		
	Bone pain and swelling	6	8.1
	Throat or neck pain	4	5.4
	Difficulty in swallowing	3	4.2
Risk factor	Long standing goiter	20	27
	Previous surgery	4	5.4
	Family history of cancer	4	5.4
	Unknown	46	60.2
Examination			
Site of thyroid swelling	Bilateral	45	60.8
	Right	15	20.3
	Left	12	16.2
	Not enlarge	2	2.7
Consistency	Firm	59	79.7
	Hard	12	16.2
	Soft	2	2.7
	Not palpable	1	1.4

Table-3: Diagnostic modalities and histological types of study participants

Variable	Parameter	Frequency	Percent %	P value
Diagnostic modalities				0.010
Thyroid status	Euthyroid	66	89.2	
	Hypothyroid	4	5.4	
	Controlled toxic	4	5.4	
Ultrasound	Multinodular	49	66.2	
	Solitary nodule	19	25.7	
	Complex	2	2.7	
	Normal	2	2.7	
	Diffuse	1	1.4	
	Cystic	1	1.4	
Radioisotope scan	Cold	63	85.1	
	Hot	7	9.5	
	Normal	4	5.4	
Histological type	Papillary	38	51.4	
	Follicular	33	44.6	
	Hurthles	3	4.6	

Table-4: DTC stage, tumor size, lymph node status, and metastasis of study participants

Variable	Parameter	Frequency	Percent %
DTC stage	Stage-1	41	55
	Stage- II	10	14
	Stage- III	7	10
	Stage-IV	16	21
Tumor size (Cm)	< 1	5	6.8
	1-2	33	44.6
	2-3	14	18.9
	3-4	15	20.3
	> 4	7	9.5
Lymph node status	Not affected	60	80.1
	Lateral compartment	8	10.8
	Lateral and central compartment	6	8.1
Metastasis			
No		56	75.7
Yes	Bone	12	16.2
	Lung	4	5.4
	Lymph nodes	2	2.7

Table-5: Type of surgery, complications, and adjuvant management of study participants

Variable	Parameter	Frequency	Percent %	P value
Type of surgery	Total thyroidectomy	38	51.4	
	Completion after lobectomy	16	21.6	
	Near total thyroidectomy	14	18.9	
	Debulking	2	2.7	
	Not done	4	5.4	
Complications				
Intraoperative		74	100	
Postoperative	Permanent vocal cord palsy	3	4.1	0.986
	Transient vocal cord palsy	2	2.7	
	Surgical site infection	1	1.4	
Adjuvant management	Radioactive iodine	47	63.4	
	Radiotherapy	6	8.1	
	Chemotherapy	1	1.4	
	Combination	13	17.6	
	Non	7	9.5	

Table-6: Gender and risk factors in relation to histological types

	Histological type				P value
Risk factors	Papillary	Follicular	Hurthles	Total	0.078
Previous surgery	2	2	0	4	
Family history of cancer	0	3	1	4	
Long standing goiter	10	8	2	20	
No risk	26	20	0	46	
Total	38	33	3	74	
Gender					
Male	11	6	1	18	0.535
Female	27	27	2	56	
Total	28	33	3	74	

DISCUSSION

Study aiming at exploring the patterns of presentation and management of differentiated thyroid cancer in the National Cancer Institute Wad Medani. Females (76%) were more likely than males (24%) to develop differentiated thyroid carcinoma, according to the male-to-female ratio (1:3.2). These findings

matched those of numerous Sudanese research, like as; According to Mohamed E *et al.*, the male to female ratio was 1.0:2.4 [5], Omran M *et al.* who documented male to female ratio was 1.0:2.5 [6], Abdelkareem A *et al.* who reported 66.1% were females and 33.9% were males [7] and Ali I *et al.* who stated 84.1% were females [8]. Also, in United Arab Emirates and Saudi

Arabia Nabil A *et al.* and Abdullah A *et al.* documented the female to male ratio was 2.4:1 and 3.5:1, respectively [9,10], in USA Lily E *et al.* revealed 77.3% of the patients were females [11]. Farah Y. also disclosed 78% of the patients were females and 22% were males with male to female ratio (1:3.5) [12]. Thyroid cancer is three times more common in women than in males, suggesting that hormonal variables may play a role in its pathogenesis. The findings of Negri *et al.* multicenter study of case-control studies demonstrated that the correlations between thyroid cancer and menstrual or reproductive variables were usually minimal; however they appeared to be greater among young women diagnosed with thyroid cancer [13]. Thyroid cancer was linked to artificial menopause and overuse of oral contraceptives; however, the link faded as time passed since the women stopped using oral contraceptives. A modest increase in risk was also observed among women who used anti-lactation medications [14]. Hormonal and reproductive variables were found to be modestly linked to thyroid cancer in later studies [15].

According to our findings, the majority of patients were between ages of 40 and 60 (45.9 %). Similarly, the average age in Sudanese studies by Mohamed E *et al.* was 51± 17 years, between the ages of 40 and 70, Omran M *et al.* identified a significant prevalence of the condition [6]. Furthermore, according to Nabil A, the total peak incidence (43.7 %) appeared in the fourth and fifth decades. Similarly, Farah Y *et al.* revealed that the patients' average age was 42.5 years. The most common symptom in our research group was anterior neck swelling, which was reported by 69 (93.2%) of the patients, followed by shortness of breath (n=15; 20.3%), and abrupt size increase (n=9; 12.2%) in more than 10% of the patients. A nodule in the thyroid area of the neck is the most common early sign of thyroid cancer. However, up to 65 % to 95 % have thyroid enlargement [16, 17].

In 20 (27 %) of our research participants, long-term goiter was the primary risk factor. Sudanese patients have a high rate of this. Iodine insufficiency might explain this; goiter is common in Sudan and other parts of Sub-Saharan Africa. Similarly, Ali I *et al.* found that long-term goiter was one of the primary risk factors for thyroid cancer in Sudanese patients [8]. Thyroid cancer was also linked to a history of long-term goiter or thyroid nodules, according to Vladan Zet [18]. Thyroid cancer can be influenced by benign thyroid illness all over the world, with goiter and benign nodules being the most powerful risk factors, with relative risks of about 3 and 30 %, respectively (43-45). The majority of the participants (45/60.8%) showed bilateral thyroid enlargement with solid consistency on examination 59 (79.7%).

Thyroid function tests revealed that the great majority of the patients in this research (66, or 89.2%)

were euthyroid. This is in line with what has been written in the past. Thyroid cancer is commonly found in euthyroid patients, however hyperthyroidism or hypothyroidism symptoms may be linked to a massive or metastatic, well-differentiated tumor [16, 17]. Furthermore, Bamidele *et al.* stated that all of the patients with thyroid cancer were euthyroid, which directly contradicts some researchers' claims that thyroid cancer displaying as thyrotoxicosis is uncommon [1].

In addition, the majority of the patients (49.6%) exhibited multinodular lesions on sonography. Similarly, Nabil A *et al.* in the UAE, Abdullah A *et al.* in Saudi Arabia, and Tadele *et al.* in Ethiopia identified multinodular lesions on ultrasonography in the majority of thyroid cancer patients, with 69 %, 59.3 %, and 47.9%, respectively [9, 10].

Papillary carcinoma was the most common kind of differentiated thyroid cancer in 38 (51.4%) patients, followed by follicular carcinoma in 33 (44.6%) patients, and Hurthles carcinoma in 3 (4.1%) patients. These findings were in line with those of Abdelkareem A *et al.* [7], Mohamed S *et al.* [20], Ala H *et al.* [21] and Ali I *et al.* those documented the most predominant type of thyroid cancer among the Sudanese population was papillary carcinoma. Also in same line, Nabil A *et al.* in United Arab Emirates [9], Lily E *et al.* in United States [11] and Tadele M *et al.* in Ethiopia [19] reported the most popular type of thyroid cancer was papillary carcinoma.

The majority of our study patients were in early stages I-II (51%) and had tumors ranging in size from 1-2 cm (44.6%), indicating early detection of DTC and, as a result, early treatment initiation. This also demonstrated good health care, appropriate diagnostic equipment, and improved patient awareness. Lily E *et al.* reported similar results, with the majority of the patients presenting in the early stages [11]. In contrast, according to Bamidele J *et al.*, Most patients with thyroid cancer who present to a referral tertiary care hospital in Cameroon are in advanced stages (stages III and IV) due to financial constraints, a lack of access to health care professionals, and a lack of appropriate medical diagnostics [1].

Metastasis was reported in 18 (24.3%) of the patients in the present study, with 12 (16.2%) of them in the bone, 4 (5.4%) in the lung, and 2 (2.4%) in the lymph nodes. Omran M *et al.* observed a similar rate of metastasis (28.6%) in Sudan, mostly in the bones [6]. In addition, Elliot Set discovered metastases in 25% of the patients, most often in the lungs and bones [22].

In terms of management, the majority of patients (38.9%) had whole thyroidectomy, 16 (21.6%) had completion following lobectomy, and 14 (18.9%) had near complete thyroidectomy. These findings are in

line with those of Omran M *et al.*, who found that complete thyroidectomy was the most common treatment option in (40%) of Sudanese patients [6].

Surgery is often suggested if a thyroid nodule needle biopsy is found to be malignant or if malignancy is suspected [23]. Similarly to our outcomes, several researches imply that a complete thyroidectomy is the preferred therapy for differentiated thyroid carcinoma [9, 24, 25].

Some researchers discovered that a complete thyroidectomy typically showed multi-centric illness and could be performed with minimum morbidity, while others showed that the more invasive technique had a survival benefit even in the low-risk group [26, 27]. The American College of Surgeons (ACS) have found after analyzing 13 years of data from the National Cancer Database (NCDB) that complete thyroidectomy leads in decreased recurrence rates and increased survival for patients with tumors larger than 1.0 cm [28].

Radioactive iodine was the most prevalent adjuvant therapy in 47 patients (63.4%), followed by radiation in 6 patients (8.1%), chemotherapy in one patient (1.4%), and combination treatment in 13 patients (17.6 %). These findings are consistent with those of Nabil A *et al.*, Abdullah A *et al.*, and Elliot S *et al.*, who found that radioactive iodine was ablated in the majority of patients after surgery [9, 10, 22].

Total thyroidectomy, radioactive iodine therapy, external irradiation, and hormone suppression are all indicated in general. Thyroid cancer can be treated with radioactive iodine therapy (RAIT), which can be utilized not only for thyroid ablation following thyroidectomy, but also for nodal and distant metastases, as well as tumor recurrence [24, 29].

Six individuals in our research suffered postoperative sequelae, including permanent vocal cord palsy in three (4.1%), transit vocal cord palsy in two (2.7%), and surgical site infection in one (1.4%). Paralysis of the recurrent laryngeal nerve or vocal cord (1-6%) (81, 82) is similar to that described in the literature. In a Sudanese research done by Mohamed E *et al.*, 9 percent of patients had vocal cord and nerve palsy [5].

CONCLUSION

According to the findings, differentiated thyroid carcinoma is more common in females and fourth-decade individuals, with long-standing goiter being a prominent risk factor. The majority of the patients had multinodular goiter and were euthyroid. The most common type was papillary carcinoma. The majority of the cases were in their early stages (I-II). The majority of patients were identified after thyroid surgery, indicating a genuine issue with preoperative

diagnosis. In local practice, the majority of patients had a complete thyroidectomy followed by radioactive iodine therapy with no cervical lymph node dissection.

RECOMMENDATIONS

- Radioiodine should be used to ablate any remaining thyroid tissues after surgery.
- The use of fine needle aspiration cytology as a gold standard investigation should be considered.
- To evaluate further outcomes among such patients, new studies with a larger sample size and a longer follow-up time are needed.
- Patients with biopsy-proven metastatic cervical lymph adenopathy should undergo therapeutic lymph node dissection.

ABBREVIATIONS

DTC: Differentiated Thyroid Cancer; HCC: Hurthle Cell Carcinoma; FNA: Fine-Needle Aspiration; LN: Lymph Node; NCI: National Cancer Institute; TNM: Tumor Size, Nodal Metastasis, Distant Metastasis; WDCT: Well-Differentiated Thyroid Cancers; ACS: American College of Surgeons; NCDB: National Cancer Database; RAIT: Radioactive iodine treatment.

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Conflicts of Interest

The authors report no conflicts of interest. Authors alone are responsible for the content and the writing of the paper.

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